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January 27, 2000

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Via Hand Delivery

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 98N-0313; Surgeon's and Patient Examination Gloves; Reclassification; Proposed Rule

On behalf of Roquette America, Inc. (Roquette), we are submitting the attached comments on the Food and Drug Administration's (FDA) July 30, 1999 proposed reclassification of Surgeon's and Patient Examination Gloves. 64 *Fed. Reg.* 41710. The original deadline for comments on this proposed rule was extended until January 27, 2000. 64 *Fed. Reg.* 58004 (October 28, 1999).

Roquette appreciates the Agency's consideration of these comments.

Sincerely,

Frederick A. Stearns

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Attachment

98N-0313

C56

ROQUETTE
America, Inc.

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Dear Sir or Madam:

Roquette America, Inc. (Roquette)[1] appreciates the opportunity to submit comments on the Food and Drug Administration's (FDA) July 30, 1999 proposed regulations concerning Surgeon's and Patient Examination Gloves. 64 *Fed. Reg.* 41710. The Agency has proposed to reclassify these products from Class I to Class II, adding two "special controls" in the form of a guidance document and additional special labeling requirements.[2] While Roquette fully supports the Agency's efforts to reduce risks associated with the use of medical devices, including those posed to persons sensitive to natural latex (NL) protein allergens, the Company believes FDA has inappropriately attributed to glove dusting powder health problems that are caused by other factors or are not currently shown to be a serious health issue. Specifically, (1) exposure to NL protein is a function of extractable protein present in latex gloves; and (2) granuloma formation (a potential issue limited primarily to surgeon's gloves) has not been shown to be a significant

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[2] As noted below, special labeling requirements for powdered surgeon's gloves have been in place since May 25, 1971 (36 Fed. Reg. 9475).

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problem in the United States in recent years, likely due to existing labeling requirements and good medical practices.

Appropriately-formulated glove dusting powders have been safely used for decades and, on balance, have provided dramatic benefits to the users of both surgeon's and patient examination gloves. Although FDA notes that a portion of the medical glove market is shifting in favor of powder-free gloves, powdered gloves will continue to make up a significant percentage of the billions of medical gloves used annually in the United States.[3] While the proposed regulation would not mandate a specific glove dusting powder limit,[4] the Agency's current discussion of glove dusting powder suggests greater risks than the cited evidence supports, and is clearly anticipated by the Agency to discourage the use of these valuable medical products.

I. The Potential for Exposure to NL Allergens is Created by Extractable NL Proteins, Not Glove Powder

As a general matter, the Agency's preamble discussion at times appears to lose sight of the fact that NL allergy concerns, a driving force behind the labeling provisions of the proposed regulations, are the result of NL proteins that extract from latex products. This is highlighted by inclusion of a proposal to require labeling synthetic surgeons and patient examination gloves with the statement: "Caution: Glove powder is associated with adverse reactions. FDA recommends that this product contain no more than 120 milligrams of powder per glove. This product contains no more than [insert level] mg powder per glove."

The Agency does not assert in the Proposed Rule that glove powder, on its own, presents an allergic reaction risk, although it makes the hedging comment that "the scientific data to define the quantitative relationship between respiratory allergic reactions and powder level on

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NL gloves are not available at this time."[5] However, the absence of such data is not surprising. Indeed, after noting several studies that linked airborne NL protein allergens to respiratory reactions, FDA specifically reported that "[t]he studies indicated that cornstarch powder not exposed to NL did not cause any reaction in sensitized subjects, while nebulized powdered NL surgeon's glove extract, and to some extent, nebulized powder-free glove extract induced bronchoconstriction in tested subjects (Ref. 31)." (64 *Fed. Reg.* at 41712) (col.3) (underlining added).

Roquette strongly urges FDA to evaluate the new studies brought to its attention in another comment.[6] These studies appear to call into question FDA's underlying conclusions (presented without reliable supporting data[7]) about the association between exposure to glove powder and respiratory health concerns.[8]

II. The Potential for Granuloma Formation is Specific to Surgeon's Gloves and the Asserted Risk is Not Supported by FDA's Adverse Event Reporting System

The preamble discussion reports that "[o]ne of the concerns regarding glove powder, in general, is its capability, as particulate material, to cause foreign body reaction, resulting in inflammation, granulomas and adhesions of peritoneal tissues after surgery (Refs. 15 to 19)." (64 *Fed. Reg.* at 41712) (col. 1-2). Notably, FDA's own Medical Device Reporting (MDR) system and Manufacturer and User Facility Device Experience Database (MAUDE) identify no

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events associating granuloma formation with glove use.[9] While recognizing that only a small fraction of adverse events are reported to FDA, it is relevant that no such glove-related granuloma/ adhesion incidents appear in these databases.

The lack of reported incidents may reflect FDA's existing labeling requirements and the diligent efforts of the medical profession. Since May 25, 1971 (36 *Fed. Reg.* 9475), FDA has required powdered surgeon's gloves to bear the statement: "Caution: After donning, remove powder by wiping gloves thoroughly with a sterile wet sponge, sterile wet towel, or other effective method."[10] The success of this cautionary labeling is borne out by the lack of adverse reports.

Similarly, although several journal articles are cited as support for this concern, closer examination of these sources shows that they do not document a current health problem with products in the United States:

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[10] Although not required, FDA encourages similar labeling for powdered patient examination gloves:

> A similar caution is recommended for powdered patient examination gloves because patient examination gloves are used in a variety of circumstances, including procedures where the surface of the glove contacts wounds, body cavities, or other possible routes of contamination. If conditions warrant, the user may wish to remove residual powder from the gloves prior to use in order to minimize the potential for adverse effects. For this reason, FDA recommends the following statement appear on each box of powdered patient examination gloves. "Caution: Users should consider the circumstances of use in deciding whether to remove powder from gloves after donning. Powder can be removed by wiping gloves thoroughly with a sterile wet sponge, sterile wet towel, or other effective method."

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The Ellis (1990) article (FDA Reference 15)[11] recounts the long history of the development and use of glove dusting powders. This author reviews numerous case reports of "starch induced peritonitis and intraperitoneal granulomas" and notes that "[m]ost of these appeared in the early 1970s, but sporadic reports have continued to be published since that time." [Ellis at 523]. The author also notes that "[i]t should be stressed that a whole variety of materials that may contaminate the peritoneal cavity at the time of operation may induce an inflammatory reaction, with consequent formation of granulomas or adhesions, or both. These include, in addition to talc and starch, gauze fluff derived from swabs, suture material, and cellulose derived from disposable gowns and drapes." [Ellis at 525] (citation omitted).

The Edlich (1994) article (FDA Reference 16)[12] recounts the author's experience with a family illness and his own subsequent professional accomplishments. The only reference to glove powder and adhesions is a citation to the Ellis (1990) paper, with no additional discussion or original data presented. This paper does not warrant a citation as separate support for FDA's concerns.

The Hunt (1994) (FDA Reference 17)[13] paper presents the results of an original study. Despite noting that "human reactions [to glove starch powder] are infrequent," the authors nevertheless conclude that "[t]here is no longer any reason to use powdered gloves in the operating room, and the fact that surgeons and hospitals now have a choice would seem to make them all the more responsible in the event of starch-induced damages to wither patients or medical staff." [Hunt at 827]. Although the authors disclaim any financial interest in the manufacturer of the one brand of powder-free

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gloves used in the study, the article notes that it was "supported by a donation from" that very company.

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The Holmdahl (1997) (FDA Reference 19)[15] article presents several "Recommendations for the reduction or prevention of adhesions." However, these recommendations appear to be based on the Ellis (1990) paper, a rat study, and the Luijendijk (1996) articles. This article does not add independent support for the Agency's powder concerns.

These citations do not demonstrate that glove powder on medical gloves, as currently labeled and used under current standards of medical practice, presents a significant risk of granuloma/foreign body reaction. As a result, FDA has not shown a need or basis for establishing reduced limits/guidelines for powder content, or for changing the existing cautionary labeling on surgeon's gloves since the existing approach is appropriate and effective. Similarly, there is no basis or need to extend such provision to patient examination gloves.

III. A Proposed Maximum Recommended Limit on Powder Content is Not Appropriate

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FDA reports test results showing glove powder levels varying between 50 mg and 426 mg per glove, with and average of 260 mg.[16] However, limited data showing some gloves with powder levels at or below 120 mg is not a reasonable basis for setting a limit, nor does it ensure that the level is attainable for different gloves (e.g., different sizes and those produced by different manufacturing methods). As noted above and in other comments, there is no established scientific basis or public health reason to impose the proposed restrictions and added cost. FDA has not adequately addressed the concern that powder reduction may adversely affect the ease of glove donning and compromise barrier properties and glove integrity.[17] These concerns are particularly applicable to synthetic patient exam gloves. In short, FDA has not presented a basis for linking glove powder to granuloma formation,[18] general "adverse health effects,"[19] or serving as a carrier for airborne allergens.[20]

IV. Conclusion

Roquette supports FDA's on-going efforts to reduce potential health risks faced by health care workers and patients from NL-containing medical devices. However, regulatory requirements should be directed toward effective mitigation of valid and substantive concerns relating to health and safety. To this end, surgeon's glove powders have long been subject of special, and effective, cautionary labeling concerning granulomas and similar foreign body reactions. FDA should not impose new requirements relating to powder cautionary statements and content for any gloves -- especially patient examination gloves.

In the case of NL allergenicity it is reasonable to consider the potential for exposure to NL allergens resulting from airborne transmission as well as from direct contact. New

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cautionary labeling regarding the presence of NL in medical products that pose an allergenicity issue[21] to certain individuals may be appropriate IF based on substantive scientific data. However, on consideration, reliable scientific data do not support (and in some cases, appear to contradict[22]) the belief that potential for exposure via airborne route merits additional cautionary labeling concerning glove powders. In fact, the labeling proposals concerning powder content will likely not have any substantive effect other than discouraging the use of powdered gloves.[23]

Linking glove powders to the NL allergenicity issue (a high-profile issue among health care workers) without a substantive scientific basis will serve only to discourage the use of an otherwise beneficial product. While alternatives to latex that do not use powders may exist, these are relatively costly and may present performance (e.g., tactile) and/or integrity issues. FDA should focus its efforts on controlling the source of the allergenic response (extractable NL protein) through appropriate means supported by reliable scientific evidence.

* * *

Roquette appreciates the Agency's consideration of these comments.

Sincerely,

John V. Fratus
Director, Regulatory Affairs

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21 FDA does not explain why the current labeling requirement found at 21 C.F.R. § 801.437 ("User labeling for devices that contain natural rubber") is not sufficient. Rather, the proposed rule would merely supersede this requirement for the specific case of medical gloves. *See* proposed revised 21 C.F.R. § 801.437(d) (64 Fed. Reg. at 41742).

22 E.g., Allegiance Comments, pages 9 – 12.

23 See 64 Fed. Reg. at 41721 (FDA projection of market share for powder-free gloves with and without the proposed regulation in effect).

ROQUETTE
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January 27, 2000

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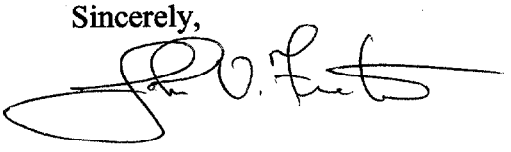
Roquette appreciates the Agency's consideration of these comments.

Sincerely,



John V. Fratus
Director, Regulatory Affairs

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21 FDA does not explain why the current labeling requirement found at 21 C.F.R. § 801.437 ("User labeling for devices that contain natural rubber") is not sufficient. Rather, the proposed rule would merely supersede this requirement for the specific case of medical gloves. *See* proposed revised 21 C.F.R. § 801.437(d) (64 Fed. Reg. at 41742).

22 E.g., Allegiance Comments, pages 9 – 12.

23 See 64 Fed. Reg. at 41721 (FDA projection of market share for powder-free gloves with and without the proposed regulation in effect).


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